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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,806	06/27/2003	Gail Isabel Reid Adam	11640-008-999	6270

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EXAMINER	
MONTANARI, DAVID A	

ART UNIT	PAPER NUMBER
1632	

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10/01/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/607,806	ADAM ET AL.	
	Examiner	Art Unit	
	David Montanari	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *24-55* is/are pending in the application.

4a) Of the above claim(s) *28,35-40 and 42-55* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24-27,29-34 and 41* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 24-27, 29-34 and 41 in the reply filed on 4/11/2008 is acknowledged.

Claims 28, 35-40 and 42-55 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/11/2008.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-27, 29-34 and 41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the

level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue" (In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The breadth of the claims encompasses identifying a candidate therapeutic for fat reduction or NIDDM by identifying any test molecule that interacts by any means with the nucleotide sequence of SEQ ID NO: 1.

The specification teaches that regarding SEQ ID NO: 1:

"It has been discovered that polymorphic variations in or near a nucleotide sequence encoding a phospholipase A2 polypeptide known as PLA2G1B, which is located on chromosome twelve, are associated with central fat deposition. In addition, it was discovered that a polymorphic variation in the same nucleotide sequence was associated with type II diabetes (non-insulin dependent diabetes mellitus, or NIDDM) in subjects. Thus, PLA2G1B has been identified as a target for reducing fat deposition and treating associated conditions, including diabetes." (pg. 2 parag. 0008).

The specification (pgs. 29 and 30 beginning at parag. 0096) goes on to describe in detail each single nucleotide polymorphism (SNP) in SEQ ID NO: 1 and what associated phenotype should be expected should the SNP be present in a sample. The specification (beginning on pg. 35) continues to teach a method of identifying a candidate therapeutic for fat reduction and NIDDM and defines "test molecule" and "candidate therapeutic" as

"modulators of regulation of transcription and translation of PLA2G1 B nucleic acids and modulations of expression and activity of PLA2G1B polypeptides. The term "modulator" as used herein refers to a molecule which agonizes or

antagonizes PLA2G 1B DNA replication and/or DNA processing (e.g., methylation), PLA2G1B RNA transcription and/or RNA processing (e.g., removal of intronic sequences and/or translocation from the nucleus), PLA2G 1B polypeptide production (e.g., translation of the polypeptide from mRNA, and/or post-translational modification such as glycosylation, phosphorylation, and proteolysis of pro-polypeptides), and/or PLA2G1B function (e.g., conformational changes, binding of nucleotides or nucleotide analogs, binding and/or translocation of ions, interaction with binding partners, effect on membrane potential, effect on fat deposition, effect on metabolic condition, and/or effect on cardiovascular condition). Test molecules and candidate therapeutics include, but are not limited to, compounds, antisense nucleic acids, ribozymes, PLA2G1B polypeptide or fragments thereof, immunotherapeutics (e.g., antibodies)" (pg. 36 parag. 00114).

However, while the specification teaches that polymorphic variations in or near a nucleotide sequence encoding a phospholipase A2 polypeptide have been discovered and mapped to particular nucleotide positions, the specification fails to teach a method of contacting any test molecule and detecting its interaction with SEQ ID NO: 1 that would suggest that the test molecule that merely interacts with PLA2G1B would be a candidate agent for fat reduction or candidate agent for NIDDM. What is problematic is that SEQ ID NO: 1 is the entire gene, 12,174 nucleotides, that only identifies the specific polymorphisms that have been linked to either fat reduction or NIDDM phenotypes. Further the specification teaches that these are "polymorphic variations in or near a nucleotide sequence encoding a phospholipase A2 polypeptide". The specification has provided no teaching what specific SNP are near or in the nucleotide sequence encoding a phospholipase A2. Since SEQ ID NO:1 is a very large sequence

and the claims are drawn to "detecting interaction" it is conceivable that many molecules may interact with any nucleotides in the 12.1 kb sequence without any effect that would designate them as a candidate therapeutic for fat reduction or NIDDM. The claims and the specification have not linked the "interaction" between the test molecule and the nucleotide sequence of SEQ ID NO: 1 that would equate that the test molecule is a candidate therapeutic for fat reduction or NIDDM. The specification has provided broad teachings of what is considered a test molecule used in the claimed method but has not taught or linked that any test molecule that interacts with the nucleic acid of SEQ ID NO: 1 would be considered a candidate therapeutic for fat reduction or NIDDM. The specification teaches that:

"the term "interaction" refers to an effect of a test molecule on a PLA2G1B nucleic acid, polypeptide, or variant thereof (collectively referred to as a "PLA2G1B molecule"), where the effect is sometimes binding between the test molecule and the nucleic acid or polypeptide, and is often an observable change in cells, tissue, or organism." parag. 0160,

however this definition of interaction is broad and encompasses a test molecule binding to any region of nucleic acid of SEQ ID NO: 1. What is not taught in the specification is that once a test molecule interacts with the nucleic acid of SEQ ID NO: 1, what should be expected of that test molecule? If a test molecule binds to nucleotides 1-100 of SEQ ID NO: 1, will that be enough for the skilled artisan to make the conclusion that the test molecule is a candidate therapeutic for fat reduction or NIDDM? Again what is missing in the specification is a nexus between the interaction of the test molecule (its specific interaction with a particular region of nucleotides in SEQ ID NO: 1) and an outcome in the resulting protein to be coded for from the sequence of SEQ ID NO: 1 that will then lead to a determination that the test molecule can be a candidate therapeutic.

The art teaches that the presence of polymorphisms in a particular nucleotide sequence does not always lead to a particular phenotype. For example Cha et al. (2002, Annals of Clinical and Lab. Sci., Vol. 32(2), pgs. 114-122) teach that the analysis of polymorphisms in the promoter of the glucose transporter (GLUT-2) in normal and NIDDM patients yields mixed results with regard to predicting outcome (see Tabled 2 pg. 118). Specifically Cha et al. teach that at positions -149, -122 and -44 SNP's do exist in both normal and NIDDM patient but address a disparity between the presence of a SNP and a diabetic phenotype by teaching:

"Of the NIDDM cases, most mutations (35 cases) were present as the A/G mixed-form at position -44, while 10 cases showed the G mutation. If the A/G mixed-form is considered heterozygotic, the G mutation may be homozygotic to the locus, raising the possibility that the human GLUT2 promoter activity may be more severely deteriorated. However, we could not find any difference in diabetic symptoms that reflected the complications arising from NIDDM in relation to A/G or G mutations." (pg. 120, col. 2 parag. 2 lines 5-15).

Thus while SNP's may exist in a particular nucleotide sequence, a predicted or correlative phenotype is not necessarily going to result because of the presence of the SNP. This is compounded in the present application because the SNP's described in SEQ ID NO: 1 are only disclosed at a particular position in the entire genomic sequence of PLA2G1B and there is no indication if this is in a particular coding sequence such as a promoter as described by Cha et al.

While Applicants have done work to demonstrate where SNPs exist in the nucleotide sequence of SEQ ID NO: 1 and linked those particular SNPs to phenotypes such as fat deposition and NIDDM, Applicants have only presented the entire human genomic sequence of SEQ ID NO:1 and provided no guidance to the skilled artisan as to what types and where interaction between a test molecule and the nucleotide sequence of SEQ ID NO: 1 would lead the skilled artisan to make the determination that test molecule would be a candidate agent for fat reduction

or candidate agent for NIDDM. Thus the skilled artisan would require and undue amount of experimentation without a predictable degree of success to make and practice the invention as claimed.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Montanari whose telephone number is (571)272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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